Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Protocol for a health technology assessment of immunisation against respiratory syncytial virus (RSV) in Ireland

Published: 28 January 2025

Table of Contents

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent statutory body established to promote safety and quality in the provision of health and social care services for the benefit of the health and welfare of the public.

Reporting to the Minister for Health and engaging with the Minister for Children, Equality, Disability, Integration and Youth, HIQA has responsibility for the following:

- **Setting standards for health and social care services** — Developing person-centred standards and guidance, based on evidence and international best practice, for health and social care services in Ireland.

- **Regulating social care services** — The Chief Inspector of Social Services within HIQA is responsible for registering and inspecting residential services for older people and people with a disability, and children's special care units.

- **Regulating health services** — Regulating medical exposure to ionising radiation.

- **Monitoring services** — Monitoring the safety and quality of permanent international protection accommodation service centres, health services and children's social services against the national standards. Where necessary, HIQA investigates serious concerns about the health and welfare of people who use health services and children's social services.

- **Health technology assessment** — Evaluating the clinical and cost effectiveness of health programmes, policies, medicines, medical equipment, diagnostic and surgical techniques, health promotion and protection activities, and providing advice to enable the best use of resources and the best outcomes for people who use our health service.

- **Health information** — Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information on the delivery and performance of Ireland's health and social care services.

- **National Care Experience Programme** — Carrying out national service-user experience surveys across a range of health and social care services, with the Department of Health and the HSE.

1 Introduction

1.1 Background

Respiratory syncytial virus (RSV) is a major contributor to acute lower respiratory tract infection (LRTI) among infants, young children and older adults. RSV is a seasonal virus; in temperate climates, outbreaks typically occur during the winter months, with the virus continuing to circulate until the early spring.[1]

Most infections in children are mild; however, in some children, RSV may progress to bronchiolitis, pneumonia and laryngotracheitis (alternatively referred to as 'croup').[2] Children at highest risk of severe RSV-associated lower respiratory tract disease (LRTD) include infants aged under six months, premature infants (that is, infants born before 37 completed weeks of gestation), children aged under two years with congenital heart or chronic lung disease, children who are immunocompromised and children with respiratory or neuromuscular disorders.[2] In older children and adults, symptoms are generally either absent or confined to the upper respiratory tract. However, older adults, those who are immunocompromised, and those with certain chronic underlying medical conditions, such as chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), diabetes and asthma, are also at increased risk of severe RSV-associated LRTD.[3] Older adults residing in long-term care facilities (LTCFs) are further identified as an important subset of the older adult population with increased susceptibility to infection and severe disease outcomes due to a combination of risk factors such as advanced age, multimorbidity, frailty and close living quarters which can contribute to the spread of infection.[4]

RSV is associated with a significant disease burden globally, resulting in considerable acute LRTI episodes, hospital admissions and in-hospital deaths. This burden is highest among children aged five years and younger, with infants aged six months and younger representing some of those at highest risk of complications.[5] There is also a significant burden among older adults.[6] The epidemiology and burden of RSV-associated disease, in Ireland and globally, has been previously described in a rapid health technology assessment (HTA) of immunisation against RSV in Ireland, published by HIQA in August 2024.[7]

In Europe, as of November 2024, there are three forms of passive immunisation authorised to protect infants against RSV infection. Two of these, palivizumab (Synagis®)[8] and nirsevimab (Beyfortus®),[9] are monoclonal antibodies. Authorisation of palivizumab is limited to those at increased risk of severe disease, specifically those born at or before 35 weeks' gestational age (wGA) and aged less than six months at the start of the RSV season, as well as children up to two years of age with haemodynamically significant congenital heart disease or requiring

treatment for bronchopulmonary dysplasia.[8] Nirsevimab is authorised for newborns and infants during their first RSV season, and for children up to two years of age who are at increased risk of severe RSV-related disease. The third product is RSVpreF (Abrysvo®),[10] a maternal vaccine administered to pregnant women during pregnancy that provides passive protection for infants from birth through six months of age. For the protection of older adults against RSV, there are currently three vaccines authorised for use in adults aged 60 years and older: RSVpreF (Abrysvo®),[10] RSVPreF3 (Arexvy®),[11] and the RSV mRNA vaccine, mRESVIA®[12].

Following a request from the Department of Health, HIQA completed a rapid HTA of alternative infant and adult immunisation strategies against RSV in Ireland, to inform an interim policy decision on the most appropriate immunisation strategy for the 2025-2026 season. The rapid HTA was published in August 2024.[7] In June 2024, the Minister for Health announced the RSV Immunisation Pathfinder Programme, which is being piloted for the 2024-2025 season.[13] Through this programme, parents of babies born from September 2024 to February 2025 are being encouraged to have their newborns immunised with nirsevimab before leaving the maternity unit. The Department of Health also requested that, following the completion of the rapid HTA, HIQA conduct a full HTA of alternative infant and adult immunisation strategies against RSV in Ireland to inform a longer-term policy decision (for the 2026-2027 season and subsequent seasons) on RSV immunisation.

This protocol outlines the planned methods for estimating the burden of disease associated with RSV in infants and older adults (aged 65 years and older) in Ireland and assessing the clinical effectiveness, cost effectiveness and budget impact of alternative strategies for the immunisation of these populations against RSV, as well as the organisational, resource, ethical, patient and social implications associated with infant and adult immunisation.

1.2 Aims and objectives

The overarching aim of this HTA is to provide advice to the Minister for Health and Health Service Executive (HSE) to inform a policy decision on the most appropriate RSV immunisation strategy for infants and or adults aged 65 years and older in Ireland for the 2026-2027 season and subsequent seasons. This advice will be provided in the context of clinical recommendations previously provided by the National Immunisation Advisory Committee (NIAC) to the Department of Health, and advice provided by HIQA to the Minister for Health and HSE to inform an interim policy decision for one season (2025-2026 season).

With respect to the immunisation of children aged less than two years identified to be at high risk of severe disease, children aged less than one year in the general

population and adults aged 65 years and older against RSV in Ireland, the objectives (that is, terms of reference) for this assessment are to:

- describe the forms of RSV immunisation authorised for use (that is, monoclonal antibodies and RSV vaccines)
- describe the epidemiology and burden of disease associated with RSV in Ireland
- describe the approach to and uptake of population-level immunisation strategies against RSV in EU/EEA countries and the UK
- review the current evidence of the clinical effectiveness and safety of authorised interventions indicated for protection against RSV
- review the methodology for economic modelling studies of RSV immunisation strategies
- assess the cost effectiveness and budget impact of alternative RSV immunisation strategies
- consider any potential organisational and resource implications of the alternative RSV immunisation strategies
- consider any ethical, patient and social implications that RSV immunisation strategies may have for individuals, the general public and the healthcare system in Ireland
- based on the findings of this assessment, provide advice to inform a decision on the most appropriate RSV immunisation strategy for the 2026-2027 and subsequent seasons.

1.3 Stakeholder engagement

1.3.1 Establishment of the expert advisory group

An appropriately representative expert advisory group (EAG) will be convened as a source of expertise to inform the interpretation of the evidence and development of the advice to the Minister for Health and HSE. This group will comprise nominees from a range of stakeholder organisations, including patient representation, healthcare providers and managers, as well as clinical, public health and methodological experts.

1.3.2 Public and targeted consultation

A public and targeted consultation will be conducted to provide a broad range of stakeholders with an opportunity to give feedback on a draft version of the report. The feedback received during the consultation and HIQA's responses to the issues raised, including any changes made to the report as a result, will be published on the HIQA website in a Statement of Outcomes report alongside the final HTA.

2 Description of technology and international practice

A description of the forms of RSV immunisation currently authorised for use (either by the EMA or the Health Products Regulatory Authority (HPRA) in Ireland) will be provided. A high-level comparison of the characteristics of the different forms of immunisation will be provided.

A review of international population-based RSV immunisation programmes in EU/EEA countries and the UK will also be undertaken to identify how such programmes are structured with respect to the population(s) to whom immunisation is offered and the immunisation strategy (for example, adult vaccination, maternal vaccination, monoclonal antibody or a combination approach for the infant population). Where available, uptake of these population-level immunisation strategies will also be described.

For Ireland, data describing the uptake of nirsevimab from the 2024-2025 RSV Immunisation Pathfinder Programme will be sought and, if available, used to inform the predicted uptake of immunisation against RSV in infants. Data from the HSE will be used to inform uptake of RSV immunisation in children aged less than two years identified to be at high risk of severe LRTD.

3 Epidemiology and burden of disease

A comprehensive description of the epidemiology of RSV and burden of disease associated with RSV in the target populations will be provided. This section will be informed by a review of national and international literature and databases. Data previously obtained to inform the HIQA rapid HTA of immunisation against RSV in Ireland published in August 2024 will be used to inform this HTA and updated, as appropriate. Given the comprehensive overview of the burden of RSV provided as part of the rapid HTA, this HTA will focus on more recent data with consideration given to changes in testing and immunisation practices.

RSV has been a notifiable disease in Ireland under the Infectious Disease Regulations since 2012. All cases should be notified to the Medical Officers of Health. Notifications are reported using the Irish Computerised Infectious Disease Reporting System (CIDR).[14] RSV activity in Ireland is monitored by the Health Protection Surveillance Centre (HPSC).[15] RSV incidence will be estimated from data obtained from the HPSC. Data from the Hospital In-Patient Enquiry (HIPE) scheme will be sought to understand the nature of RSV hospitalisations (for example, complications of the disease, hospital length of stay, and the average cost of admissions).[16] Cross-sectional analyses of nationally representative datasets and individual studies will be used, if deemed appropriate. Where there is an absence of Irish data, the best available estimates will be derived from international literature.

Estimation of the eligible population

The most recent Irish census data from the Central Statistics Office will be used to estimate the size of the eligible populations of infants and older adults. Given the established policy of offering RSV immunisation with a monoclonal antibody to infants aged less than two years at high risk of severe LRTD during their first and second RSV seasons, the HSE data will be used to estimate the size of this eligible population. For the older adult population at increased risk of severe disease due to the presence of underlying medical conditions, data will be sought from existing adult immunisation programmes where relevant subgroups have eligibility.

4 Clinical efficacy, effectiveness and safety

Up-to-date evidence underpinning the use of RSV immunisation is central to decision-making regarding the expansion of the national immunisation programme. Accordingly, four research questions (RQs) have been formulated to establish the clinical efficacy, effectiveness and safety of RSV immunisation products.

RQ 1 — What is the clinical efficacy and effectiveness of the currently authorised RSV monoclonal antibodies (for the prevention of RSV and associated complications) in infants in the general population and in children aged less than two years at increased risk of severe disease?

RQ 2 — What is the safety profile of the currently authorised RSV monoclonal antibodies, when used for the prevention of RSV and associated complications, in infants in the general population and in children aged less than two years at increased risk of severe disease?

RQ 3 — What is the clinical efficacy and effectiveness of the currently authorised RSV vaccines for the prevention of RSV and associated complications in infants (through maternal vaccination) and in adults aged 65 years and older?

RQ 4 — What is the safety profile of the currently authorised RSV vaccines when used for the prevention of RSV and associated complications in infants (through maternal vaccination) and in adults aged 65 years and older?

The assessment of clinical efficacy, effectiveness and safety will be informed by systematic reviews of the literature. The specific PICOS (population, intervention, comparator, outcomes and study design) for this HTA are presented in Table 1.

Table 1: PICOS for clinical effectiveness and safety of different RSV immunisation strategies

Population	Infants, children (aged less than two years at increased risk of severe disease), pregnant women and older adults (65 years of age and older)
Intervention	**One** of the following forms of authorised RSV immunisation: **RSV monoclonal antibodies:** ○ Nirsevimab (Beyfortus®) **RSV vaccines:** ▪ Pregnant women ○ RSVpreF (Abrysvo®) ▪ Older adults ○ RSVpreF (Abrysvo®) ○ RSVPreF3 (Arexvy®) ○ mRNA vaccine (mResvia®)
Comparator	▪ No immunisation ▪ Placebo ▪ Co-administration with another vaccine ▪ Another authorised form of RSV immunisation (head-to-head comparison with RSV vaccine OR RSV monoclonal antibodies)
Outcomes	**Efficacy or effectiveness — main outcomes** ▪ RSV infection (laboratory-confirmed*) ▪ RSV-related outpatient medically attended lower respiratory tract infection (MALRI) (laboratory-confirmed*) ▪ RSV-related hospitalisation including duration of hospitalisation (laboratory-confirmed*) ▪ RSV-related ICU admission (laboratory-confirmed*) ▪ RSV-related death (laboratory-confirmed*)

	Efficacy or effectiveness — additional outcomes ▪ Duration of protection (against any of the above-mentioned outcomes) ▪ Duration of stay in ICU ▪ Duration of invasive ventilation ▪ Patient-reported outcomes and quality of life ▪ Antibiotic use for lower respiratory tract infection ▪ Long-term outcomes: ○ Development of asthma (children) ○ Reduced functional capacity (adults) **Safety — main outcomes** ▪ Serious adverse events[+] related to vaccination or immunisation including neurological disorders such as Guillain-Barré syndrome ▪ Safety — additional outcomes ▪ All adverse events, including: ○ Solicited adverse events — local and systemic reactions ○ Unsolicited adverse events — spontaneously reported/ other adverse events ▪ Adverse pregnancy outcomes after vaccination during pregnancy[¥] ▪ Adverse neonatal outcomes after vaccination during pregnancy[^]
Study design	High-quality systematic reviews[§] of randomised controlled trials and non-randomised studies with a control group

Key: ICU — intensive care unit; PCR — polymerase chain reaction; RSV — respiratory syncytial virus.
[*]A positive laboratory diagnosis by PCR, virus culture or antigen detection.
[+]An adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a birth defect.[(17)]
[¥] Spontaneous abortion, foetal death, stillbirth, preterm birth (less than 37 weeks), pre-eclampsia and eclampsia.
[^] Congenital malformations (minor and major), neonatal death, and small-for-gestational-age.
[§] As described in Section 4.1

4.1 Identification of systematic reviews

In the interests of efficiency, evidence from high-quality, recently published systematic reviews of the clinical effectiveness and safety of RSV monoclonal antibodies and vaccines will be used to address these research questions, where available. This reflects a pragmatic approach to evidence synthesis, consistent with the hierarchy of evidence, wherein duplication of effort is minimised. For the purpose of this evidence review, a high-quality systematic review is considered to comprise reviews reporting on at least one outcome of interest with all of the following characteristics:

- a clearly stated set of objectives with an explicit, reproducible methodology
- a systematic search of at least two databases, which attempts to identify all studies that would meet the eligibility criteria
- a systematic presentation and synthesis of the characteristics and findings of the included studies
- a critical appraisal of the available evidence
- ideally, the systematic review will have evaluated the certainty of the evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.[18]

It is noted that the European Centre for Disease Prevention and Control (ECDC) issued a tender for a systematic review of the efficacy, effectiveness and safety of monoclonal antibodies for the prevention of RSV in infants and children. It has also issued a tender for a systematic review of the efficacy, effectiveness and safety of RSV vaccines. The protocols for these reviews are published on PROSPERO.[19, 20] The HIQA evaluation team intends to use these ECDC systematic reviews to inform the HTA rather than duplicating this research. Two reviewers will independently appraise the quality of the reviews using the AMSTAR 2 tool (A Measurement Tool to Assess Systematic Reviews, version 2). Consideration will be given to updating these reviews, if necessary.

5 Costs and economics

An economic evaluation, comprising a cost-effectiveness analysis (CEA), and a budget impact analysis (BIA) will be conducted. While the 'reference case' or preferred method in the primary analysis for HTA in Ireland is to adopt the perspective of the publicly funded health and social care system (HSE), the national HTA guidelines state that it may be appropriate to adopt a wider societal perspective if clearly justified and supported by sufficient evidence.[21] Elements relating to immunisation strategies that may be undervalued when a payer perspective is adopted include the prevention of complications, health gains for caregivers, community immunity and or benefits, enhanced productivity and the promotion of equity.[22] Consideration will therefore be given to also conducting the CEA from the societal perspective following review of the evidence for indirect or societal effects.

5.1 Methodology for economic modelling studies

A preliminary scoping of the literature was undertaken to review approaches used for economic modelling of RSV immunisation. A systematic review was identified that contained searches up until October 2020, prior to the authorisation of recently licensed forms of immunisation against RSV.[23] Considering the methodology from

this 2020 review, a rapid review of economic modelling studies will be conducted including searches from October 2020 onwards to inform the model structure and parameter inputs of an Irish-specific CEA. The electronic search strategy for the rapid review was developed by a librarian and peer reviewed by a second librarian using the PRESS tool. The electronic search strategy for all databases is available on Zenodo.[24] The specific PICo for the review is outlined in Table 2.

Table 2: PICo for a rapid review of methodology for respiratory syncytial virus (RSV) immunisation economic modelling studies

Population	Young children and or adults in the general population being immunised against RSV
Interest	Approaches to modelling the expected costs and benefits of RSV immunisation in children and or adults, including, but not limited to: ▪ Model structure ○ Type of model ○ Perspective adopted ○ Time horizon ○ Discount rate for costs and outcomes ○ Age at immunisation ○ Dosing schedule ○ Immunisation type (i.e., vaccine and or monoclonal antibody) ○ Comparator ○ Waning immunity ▪ Model input parameters ○ Immunisation efficacy and or effectiveness ○ Immunisation coverage ○ Direct and indirect costs ○ Direct and indirect benefits ○ Utility values for cost-utility analysis ▪ Model outputs ○ Economic model results that include a ratio of (incremental) costs to (incremental) benefits or net monetary benefit (NMB) ○ Epidemiological model outputs used in a related economic model
Context	RSV immunisation in high-income countries (as defined by the OECD)*

Key: OECD — Organisation for Economic Cooperation and Development; RSV — respiratory syncytial virus

*OECD: WDI - The World by Income and Region (worldbank.org)

5.2 Cost-effectiveness analysis (CEA)

The CEA of immunisation of infants and or adults against RSV will be conducted in line with national HTA guidelines and reported in accordance with Consolidated Health Economic Evaluation Reporting Standards (CHEERS 2022) reporting guidelines.[21, 25] It will be conducted from the perspective of the publicly funded healthcare system (that is, the HSE), with consideration also given to the presentation of the societal perspective. The primary outcome of the CEA will be an incremental cost-effectiveness ratio (ICER) expressed in terms of the mean cost per quality-adjusted life year (QALY) gained. A discount rate of 4% will be applied to costs and outcomes occurring after the first year. There is currently no accepted willingness-to-pay (WTP) threshold for health technologies in Ireland. However, WTP thresholds of €20,000/QALY and €45,000/QALY are generally employed to interpret evidence of cost effectiveness.

A total of 13 different considerations have been identified for modelling and health economic evaluation of vaccines and immunisation programmes specifically. These include:

- model selection (static or dynamic)
- time horizon of models
- natural disease history
- measures of vaccine-induced protection
- duration of vaccine-induced protection
- indirect effects apart from herd protection
- target population
- model calibration and validation
- handling uncertainty
- discounting
- health-related quality of life
- cost components
- the perspective adopted.[26]

The model structure that is employed will be informed by the results of the review of economic modelling studies.

Comparator

As noted in Section 1.1, a pathfinder programme has been implemented for the 2024-2025 RSV season that offers nirsevimab to all infants born between 1 September 2024 and 28 February 2025. Moreover, a rapid HTA was undertaken to inform a decision by the Department of Health in relation to RSV immunisation for infants and older adults for the 2025-2026 RSV season. However, no policy decision

has been made with respect to future years. Therefore, the comparator considered in this assessment is that there is no RSV immunisation offered to the general infant or older adult population; instead, immunisation is limited to offering a monoclonal antibody to infants and children up to two years of age at high risk of severe LRTD during their first and second RSV season. The short-acting monoclonal antibody, palivizumab, was historically used; however, this policy was updated for the 2024-2025 RSV season to the provision of the long-acting monoclonal antibody nirsevimab in line with NIAC recommendations and advice from HIQA's rapid HTA.

Intervention

The following strategies are framed in the context of the RSV season in Ireland. For the purpose of the economic model, it is assumed that the RSV season comprises the period September to February — a six-month period. Therefore, for example, babies born in the RSV season will comprise those born between September and February, inclusive, while those born outside the season will comprise those born between March and August, inclusive. It is recognised that the timing of the RSV season may vary and is informed by year-round surveillance by the HPSC in collaboration with the National Virus Reference Laboratory.

Considering the population of infants aged 0 to 12 months during their first RSV season, the following strategies for immunisation of infants will be modelled:

i) **seasonal monoclonal antibody strategy**, with nirsevimab offered at birth to those born during the RSV season

ii) **seasonal plus catch-up monoclonal antibody strategy**, with nirsevimab offered at birth to those born during the RSV season (per strategy i above) and as a catch up in the first month of the season to those infants born prior to the RSV season

iii) **seasonal maternal vaccination strategy**, with the maternal vaccine offered to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season

iv) **combination seasonal strategy** providing seasonal maternal vaccination to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, with nirsevimab offered to infants born during the season who are not protected by maternal vaccination (that is, infants born to mothers for whom there is either no record of maternal vaccination or who are born within two weeks of maternal vaccination)

v) **combination seasonal plus catch up strategy** providing seasonal maternal vaccination to pregnant women between 24 and 36 weeks' gestation where the estimated due date falls during the RSV season, with nirsevimab offered to all other infants during their first RSV season, that is:
   - to infants born during the season who are not protected by maternal vaccination (that is, infants born to mothers for whom there is either no record of maternal vaccination or who are born within two weeks of maternal vaccination)
   - as a catch up in the first month of the season to those infants born prior to the RSV season according to strategy ii above (seasonal plus catch-up monoclonal antibody).

For adults aged 65 years and older, the following strategies will be modelled:

i) **single-dose vaccination** offered in the weeks prior to the anticipated onset of the RSV season to the general population aged 65 years and older disaggregated by five-year age band as follows: 65 to 69 years, 70 to 74 years, 75 to 79 years, 80 years and older.

Estimates of the relative effectiveness of potential immunisation strategies generated from the review of clinical effectiveness and safety will be used to populate the economic model. Where possible, model inputs will be informed by national literature and data sources, including those detailed in Section 3. In the absence of robust national data, data from countries considered to be generalisable to the Irish setting may be a potential source of model input values. Where data from the literature are lacking or subject to considerable uncertainty, the input of the EAG will be sought to inform suitable model input parameters.

Sensitivity and scenario analyses will be conducted to explore the key sources of uncertainty and how they impact on the conclusions of the economic analysis. This includes accounting for parameter uncertainty (for example, costs), methodological uncertainty (for example, transmission dynamics) and model uncertainty. Additionally, there are a number of vaccine-specific features that require consideration in uncertainty analysis, including but not limited to, duration of immunity, vaccination coverage, and the need for boosting. Based on the findings of the review of economic modelling studies and input of the EAG, the key drivers of uncertainty will be examined in scenario analyses.

5.3 Budget impact analysis (BIA)

The BIA will provide information for policy-makers regarding the potential affordability of different strategies for the immunisation of infants and or adults

against RSV. The BIA for each of the immunisation strategies will be presented relative to current care (that is, immunisation limited to infants, and children at high risk of severe LRTD during their first and second RSV seasons). In addition to the strategies identified for the CEA analysis, the budget impact of offering once-off vaccination to subsets of the older adult population who are at increased risk of severe disease, as per the NIAC recommendations, will be examined. Specifically, the BIA will also be presented for those aged 65 years and older:

- with significant comorbidities
- living in long-term care facilities.

The analysis will estimate the costs to the HSE associated with implementing the immunisation programme over an initial five-year time horizon, reported in terms of incremental annual cost, for the 2026-2027 RSV season and subsequent seasons. Estimates of budget impact will be particularly sensitive to uptake rates for the immunisation strategies. A range of scenarios reflecting judgements on uptake rates for immunisation will therefore be considered in the BIA. For parameters that are unsupported by the published literature, input from the EAG will be required to inform plausible values. In addition to the cost of the monoclonal antibodies and vaccines, changes to organisational processes will be identified and considered as part of the BIA. Furthermore, potential cost offsets, such as prevention of disease sequelae and hospitalisation, will be considered and included, if appropriate.

A summary of the model characteristics for each of the CEA and BIA is presented in Table 3.

Table 3: Model characteristics for CEA and BIA

Model characteristics	CEA	BIA
Perspective	Publicly funded health and social care system (HSE)	Publicly funded health and social care system (HSE)
Time horizon	Lifetime‡	Five years‡
Discount rate	4% (costs and QALYs)* after the first year	N/A
Outcome	ICER or incremental net monetary benefit (INMB)	Incremental cost per annum
Sensitivity analysis	Probabilistic and deterministic	Deterministic

Key: BIA — budget impact analysis; CEA — cost-effectiveness analysis; HSE — Health Service Executive; ICER — incremental cost-effectiveness ratio; N/A — not applicable; QALY — quality-adjusted life year.
*Or the discount rate that applies at the time of publication.
‡The time horizon for the analysis may be dependent on input parameters for clinical effectiveness and safety estimates which will be based on evidence from the systematic review.

6 Organisational considerations

The assessment of necessary organisational changes will be carried out in accordance with the EUnetHTA Core Model.[27] This assessment will include the impact of the alternative immunisation strategies on various types of resources (such as human resources, equipment and supplies, and facilities) and any additional associated healthcare interventions (for example, additional patient and or parent/guardian education and support services) for the target populations.

7 Ethical, patient and social aspects

There are many factors that need to be considered prior to the implementation of a health technology. This chapter will examine the patient, social and ethical considerations relating to a decision to provide immunisation against RSV to infants and or older adults. In the context of this chapter, 'patient aspects' will refer to issues such as the burden, experiences and expectations that are relevant to patients, individuals and carers. The term 'social aspects' refers to issues experienced by groups or communities of patients or individuals that may be relevant to the topic under assessment.[27] The ethical analysis will consider key

social and moral norms and values relevant to immunisation programmes. Key ethical issues, as outlined in the EUnetHTA Core Model, will be used to guide the ethical analysis, under some or all of the following topic headings:[27]

- benefit-harm balance at both the individual and population level
- autonomy
- respect for persons
- justice and equity
- legislation
- ethical consequences.

8 Dissemination

The evidence gathered, as outlined above, will be synthesised in a report to be published on the HIQA website. The findings of the report will inform HIQA's advice to the Minster for Health and the HSE.

References

1. Du Y, Yan R, Wu X, Zhang X, Chen C, Jiang D, et al. Global burden and trends of respiratory syncytial virus infection across different age groups from 1990 to 2019: A systematic analysis of the Global Burden of Disease 2019 Study. Int J Infect Dis. 2023;135:70-6.
2. Jha A, Jarvis H, Fraser C, PJM. O. SARS, MERS and other Viral Lung Infections: Chapter 5 Respiratory Syncytial Virus [Internet]. Sheffield (UK): European Respiratory Society; 2016 [updated 2016 June 1; cited 2024 August 26]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK442240/.
3. Kaler J, Hussain A, Patel K, Hernandez T, Ray S. Respiratory Syncytial Virus: A Comprehensive Review of Transmission, Pathophysiology, and Manifestation. Cureus. 2023;15(3):e36342.
4. Childs A, Zullo AR, Joyce NR, McConeghy KW, van Aalst R, Moyo P, et al. The burden of respiratory infections among older adults in long-term care: a systematic review. BMC Geriatr. 2019;19(1):210.
5. Li Y, Wang X, Blau DM, Caballero MT, Feikin DR, Gill CJ, et al. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in children younger than 5 years in 2019: a systematic analysis. Lancet (London, England). 2022;399(10340):2047-64.
6. Savic M, Penders Y, Shi T, Branche A, Pirçon JY. Respiratory syncytial virus disease burden in adults aged 60 years and older in high-income countries: A systematic literature review and meta-analysis. Influenza Other Respir Viruses. 2023;17(1):e13031.
7. Health Information and Quality Authority. Rapid health technology assessment of immunisation against respiratory syncytial virus (RSV) in Ireland [Internet]. HIQA; 2024 [updated 2024 August 13; cited 2024 August 26]. Available from: https://www.hiqa.ie/reports-and-publications/health-technology-assessment/rapid-health-technology-assessment.
8. European Medicines Agency. Synagis: EPAR - Summary of Product Characteristics [Internet]. European Medicines Agency; 2009 [updated 2023 October 11; cited 2024 August 26]. Available from: https://www.ema.europa.eu/en/documents/product-information/synagis-epar-product-information_en.pdf.
9. European Medicines Agency. Beyfortus: EPAR - Summary of Product Characteristics [Internet]. European Medicines Agency; 2022 [updated 2024 October 16; cited 2024 November 27]. Available from: https://www.ema.europa.eu/en/documents/product-information/beyfortus-epar-product-information_en.pdf.
10. European Medicines Agency. Abrysvo: EPAR - Summary of Product Characteristics [Internet]. European Medicines Agency; 2023 [updated 2024 September 10; cited 2024 November 27]. Available from: https://www.ema.europa.eu/en/documents/product-information/abrysvo-epar-product-information_en.pdf.
11. European Medicines Agency. Arexvy: EPAR - Summary of Product Characteristics [Internet]. European Medicines Agency; 2023 [updated 2024 October 09; cited 2024 November 27]. Available from: https://www.ema.europa.eu/en/documents/product-information/arexvy-epar-product-information_en.pdf.
12. European Medicines Agency. mRESVIA: EPAR - Summary of Product Characteristics [Internet]. European Medicines Agency; 2024 [updated 2024 September 06; cited 2024 November 27]. Available from: https://www.ema.europa.eu/en/documents/product-information/mresvia-epar-product-information_en.pdf.
13. Department of Health. Press Release: Minister for Health announces government approval for a new Respiratory Syncytial Virus (RSV) Immunisation Pathfinder Programme [Internet]. Department of Health; 2024 [updated 2024 October 10; cited 2024 November 27]. Available from: https://www.gov.ie/en/press-release/b0e06-minister-for-health-announces-government-approval-for-a-new-respiratory-syncytial-virus-rsv-immunisation-pathfinder-programme/.
14. Health Protection Surveillance Centre. Respiratory Virus Notification Data Hub. Epidemiology of Respiratory Syncytial Virus (RSV) in Ireland. [Internet]. HPSC; 2023 [cited 2024 November

27]. Available from: https://respiratorydisease-hpscireland.hub.arcgis.com/pages/rsv.
15. Health Protection Surveillance Centre. RSV Factsheet [Internet]. HPSC; 2024 [updated 2024 August 20; cited 2024 August 26]. Available from: https://www.hpsc.ie/a-z/respiratory/respiratorysyncytialvirus/factsheet/.
16. Healthcare Pricing Office. Hospital In-patient Enquiry Scheme (HIPE) [Internet]. Dublin: HPO; 2024 [cited 2024 November 27]. Available from: https://www.hpo.ie/.
17. European Medicines Agency. Glossary - serious adverse reaction [Internet]. European Medicines Agency; 2024 [cited 2024 November 27]. Available from: https://www.ema.europa.eu/en/glossary-terms/serious-adverse-reaction.
18. Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. [Internet]. The GRADE Working Group; 2013 [updated 2013 October2024]. Available from: https://guidelinedevelopment.org/handbook.
19. Saif-Ur-Rahman K, King C, Whelan S, Blair M, Donohue S, Madden C, et al. Efficacy, effectiveness and safety of respiratory syncytial virus vaccines. PROSPERO - International prospective register of systematic reviews. 2023.
20. Taneri PE, McCarthy K, O'Hagan S, Saif-Ur-Rahman K, Kothari K, Dwan K, et al. Authorised Extended Half-life Monoclonal Antibodies for Respiratory Syncytial Virus Prevention in Infants and Children: a Systematic Review Protocol. PROSPERO - International prospective register of systematic reviews. 2024.
21. Health Information and Quality Authority. Guidelines for the Economic Evaluation of Health Technologies in Ireland [Internet]. HIQA; 2020 [updated 2020 September 28; cited 2024 August 26]. Available from: https://www.hiqa.ie/reports-and-publications/health-technology-assessment/guidelines-economic-evaluation-health.
22. Annemans L, Beutels P, Bloom DE, De Backer W, Ethgen O, Luyten J, et al. Economic Evaluation of Vaccines: Belgian Reflections on the Need for a Broader Perspective. Value Health. 2021;24(1):105-11.
23. Treskova M, Pozo-Martin F, Scholz S, Schönfeld V, Wichmann O, Harder T. Assessment of the Effects of Active Immunisation against Respiratory Syncytial Virus (RSV) using Decision-Analytic Models: A Systematic Review with a Focus on Vaccination Strategies, Modelling Methods and Input Data. PharmacoEconomics. 2021;39(3):287-315.
24. Carrigan M. Zenodo - HIQA Repsitory: Search strategies for a rapid review for economic modelling studies on RSV immunisation [Internet]. 2024 [cited 2024 November 27]. Available from: https://zenodo.org/records/14178300.
25. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value Health. 2022;25(1):3-9.
26. Ultsch B, Damm O, Beutels P, Bilcke J, Brüggenjürgen B, Gerber-Grote A, et al. Methods for Health Economic Evaluation of Vaccines and Immunization Decision Frameworks: A Consensus Framework from a European Vaccine Economics Community. Pharmacoeconomics. 2016;34(3):227-44.
27. European Network for Health Technology Assessment. EUnetHTA Joint Action 2, Work Package 8 Deliverable - HTA Core Model Version 3.0 [Internet]. EUnetHTA; 2016 [updated 2016 Jan 25; cited 2024 August 26]. Available from: https://www.eunethta.eu/wp-content/uploads/2018/03/HTACoreModel3.0-1.pdf.

Published by the Health Information and Quality Authority (HIQA).

For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y

+353 (0)1 8147400

info@hiqa.ie

www.hiqa.ie